**Citation:**

Tanasescu M, Cho E, Manson JE, Hu FB. Dietary fat and cholesterol and the risk of cardiovascular disease among women with type 2 diabetes. *Am J Clin Nutr.* 2004 Jun;79(6):999-1005.

**PubMed ID:** 15159229

**Study Design:**

Prospective Cohort Study

**Class:**

B - Click here for explanation of classification scheme.

**Research Design and Implementation Rating:**

POSITIVE: See Research Design and Implementation Criteria Checklist below.

**Research Purpose:**

To assess the relationship between different types of dietary fat and cholesterol and the risk of CVD among women with type 2 diabetes.

**Inclusion Criteria:**

- Female nurses between the ages of 30-55 years (in 1976) partaking in the Nurses' Health Study
- Reported a physician's diagnosis of diabetes mellitus at age ≥30 years on any questionnaire between 1976 and 1996 using the National Diabetes Data Group diagnostic criteria for the diagnosis of diabetes.

**Exclusion Criteria:**

- Women with a history of MI, angina, coronary revascularization, stroke or cancer at baseline
- Women who had a CVD event during a previous 2-year interval were excluded from subsequent follow-up.

**Description of Study Protocol:**

**Recruitment:** All female nurses who participated in the Nurses' Health Study between 1976 and 1996 who reported on any questionnaire between 1976 to 1996 a physicians' diagnosis of diabetes mellitus at age ≥30 years.

**Design:** Prospective cohort study

**Blinding used (if applicable):** Implied for data analysis

**Intervention (if applicable):** Not applicable

**Statistical Analysis:**

- Correlation coefficients used to measure the trend for total and specific types of fat assessed by dietary records
- Median value used to test for trends for increasing categories of nutrient or food intake
- Multivariate Cox proportional hazard models used for energy intake, percentage of energy derived from protein and specific types of fat and potentially confounding variable alcohol intake, smoking, family history of MI, use of vitamin E supplements, use of multivitamin supplements, quintiles of dietary fiber, hours spent per week in moderate or vigorous physical activity, diabetes medication, BMI and menopausal status.

**Data Collection Summary:**

**Timing of Measurements:**

- The Nurses' Health Study started in 1976 with follow-up questionnaires sent every 2 years until 1996
- All women qualifying for the study were sent a supplementary questionnaire on symptoms, diagnosis and treatment (unclear when these questionnaires were sent)

- A 61-food item semiquantitative food-frequency questionnaire (FFQ) was mailed to women in the cohort in 1980
- The FFQ was expanded to 116 food items in 1984 and was updated in 1986, 1990 and 1994

**Dependent Variables**

- Risk of cardiovascular disease

**Independent Variables**

- Dietary fat (saturated, polyunsaturated and monounsaturated) and dietary cholesterol intake assessed through semiquantitative food frequency questionnaires

**Control Variables**

- Energy intake
- Percentage of energy derived from protein and specific types of fat
- Alcohol intake
- Smoking
- Family history of myocardial infarction
- Use of vitamin E supplements
- Use of multivitamin supplements
- Quintiles of dietary fiber
- Hours spent per week in moderate or vigorous physical activity
- Diabetes medication
- BMI
- Menopausal status.

**Description of Actual Data Sample:**

**Initial N:** 5674 women

**Attrition (final N):** 5672 women (reported numbers different in article)

**Age:** 30-55 years old

**Ethnicity:** Predominantly white women; however, ethnic breakdown not stated in article.

**Other relevant demographics:** None mentioned

**Anthropometrics:** Groups were similar - adjustments were made for age

**Location:**

- Original NHS data collected from nurses residing in California, Connecticut, Florida, Maryland, Massachusetts, Michigan, New Jersey, New York, Ohio, Pennsylvania and/or Texas
- Data collection completed at the Departments of Nutrition and Epidemiology, Harvard School of Public Health, the Channing Laboratory, Boston, and the Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston.

**Summary of Results:**

**Key Findings**

- Between 1980 and 1998, 619 new cases of CVD (nonfatal myocardial infarction, fatal coronary heart disease, and stroke) were identified
- The relative risk of CVD for an increase of 200 mg cholesterol/1000 kcal was 1.37 (95% CI: 1.12, 1.68, P = 0.003).
- Each 5% of energy intake from saturated fat, as compared with equivalent energy from carbohydrates, was associated with a 29% greater risk of CVD (RR = 1.29, 95% CI: 1.02, 1.63, P = 0.04).
- The P:S ratio (polyunsaturated to saturated fat) was inversely associated with the risk of fatal CVD.
- Replacement of 5% of energy from saturated fat with equivalent energy from carbohydrates or monounsaturated fat was associated with a 22% or 37% lower risk of CVD, respectively.

| Fat Variables | Age-adjusted RR | *P* | Multivariate RR | *P* |
|---|---|---|---|---|
| Total fat (each increase of 5% energy) | 1.05 (0.99, 1.11) | 0.10 | 1.01 (0.94, 1.08) | 0.79 |
| Animal fat (each increase of 5% energy) | 1.09 (1.03, 1.14) | 0.001 | 1.01 (0.94, 1.09) | 0.74 |

| | | | | |
|---|---|---|---|---|
| Vegetable fat (each increase of 5% energy) | 0.88 (0.08, 0.96) | 0.004 | 0.93 (0.82, 1.06) | 0.26 |
| Saturated fat (each increase of 5% energy) | 1.19 (1.06, 1.34) | 0.003 | 1.29 (1.02, 1.63) | 0.04 |
| Monounsaturated fat (each increase of 5% energy) | 1.11 (0.99, 1.24) | 0.08 | 0.81 (0.63, 1.04) | 0.10 |
| Polyunsaturated fat (each increase of 5% energy) | 0.92 (0.70, 1.21) | 0.57 | 0.97 (0.68, 1.39) | 0.86 |
| *trans* Unsaturated fat (each increase of 2% energy) | 1.21 (0.96, 1.53) | 0.12 | 1.20 (0.84, 1.72) | 0.32 |
| Cholesterol (each increase of 200 mg/1000 kcal) | 1.55 (1.31, 1.83) | <0.001 | 1.37 (1.12, 1.68) | 0.003 |
| P:S (each increase of 0.1 unit) | 0.93 (0.87, 0.98) | 0.01 | 0.94 (0.87, 1.01) | 0.10 |
| Keys score (each increase of 10) | 1.18 (1.10, 1.27) | <0.001 | 1.23 (1.08, 1.40) | 0.002 |

Table shows the relative risks (RRs) of cardiovascular disease according to fat intake, cholesterol and Keys score among diabetic women. All fat variable were introduced as continuous predictors. $n$ = 5672; person-years = 57,195. P:S = ratio of polyunsaturated to saturated fat.

**Other Findings:**

- The P:S was strongly inversely related to fatal events, but was not related to nonfatal events.
- The Keys score was positively related to fatal events but not to nonfatal events.
- There were no major differences in the relationship between types of fat and CVD risk among women with diabetes at baseline (prevalent cases) and among women who became diabetic during the follow-up (incident cases)
- *trans f*at intake was associated with a nonsignificant increase in CVD risk among incident cases (RR: 1.49; 95% CI: 0.86, 2.57 for 2% of energy;$P$ = 0.15) but not among prevalent cases (RR: 0.95; 95% CI : 0.59, 1.58; $P$ = 0.84).

**Author Conclusion:**

In conclusion, in this prospective cohort study of diabetic women, we found that higher saturated fat and cholesterol intakes were significantly associated with CVD risk. A higher P:S ratio was associated with a lower risk of fatal events. Thus, among diabetic persons, it is important to reduce intakes of cholesterol and to replace saturated fats with unhydrogenated unsaturated fats.

Monounsaturated fat (MUFA) may be more effective in decreasing risk of CVD than carbohydrates as a replacement for saturated fat in diabetic subjects.

***Reviewer Comments:***

*The author notes that because of the relatively small sample size, the CIs were wide for the estimates.*

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***Research Design and Implementation Criteria Checklist: Primary Research***

**Relevance Questions**

| | | |
|---|---|---|
| 1. | Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies) | Yes |
| 2. | Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about? | Yes |
| 3. | Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice? | Yes |
| 4. | Is the intervention or procedure feasible? (NA for some epidemiological studies) | Yes |

**Validity Questions**

| | | |
|---|---|---|
| **1.** | **Was the research question clearly stated?** | Yes |
| 1.1. | Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified? | Yes |

| | | |
|---|---|---|
| 1.2. | Was (were) the outcome(s) [dependent variable(s)] clearly indicated? | Yes |
| 1.3. | Were the target population and setting specified? | Yes |
| **2.** | **Was the selection of study subjects/patients free from bias?** | Yes |
| 2.1. | Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study? | Yes |
| 2.2. | Were criteria applied equally to all study groups? | N/A |
| 2.3. | Were health, demographics, and other characteristics of subjects described? | Yes |
| 2.4. | Were the subjects/patients a representative sample of the relevant population? | Yes |
| **3.** | **Were study groups comparable?** | Yes |
| 3.1. | Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT) | N/A |
| 3.2. | Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline? | N/A |
| 3.3. | Were concurrent controls used? (Concurrent preferred over historical controls.) | N/A |
| 3.4. | If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis? | Yes |
| 3.5. | If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.) | N/A |
| 3.6. | If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")? | N/A |
| **4.** | **Was method of handling withdrawals described?** | No |
| 4.1. | Were follow-up methods described and the same for all groups? | Yes |
| 4.2. | Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.) | No |
| 4.3. | Were all enrolled subjects/patients (in the original sample) accounted for? | No |
| 4.4. | Were reasons for withdrawals similar across groups? | N/A |
| 4.5. | If diagnostic test, was decision to perform reference test not dependent on results of test under study? | N/A |
| **5.** | **Was blinding used to prevent introduction of bias?** | Yes |
| 5.1. | In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate? | N/A |
| 5.2. | Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.) | Yes |
| 5.3. | In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded? | Yes |
| 5.4. | In case control study, was case definition explicit and case ascertainment not influenced by exposure status? | N/A |
| 5.5. | In diagnostic study, were test results blinded to patient history and other test results? | N/A |

| | | |
|---|---|---|
| **6.** | **Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?** | Yes |
| 6.1. | In RCT or other intervention trial, were protocols described for all regimens studied? | N/A |
| 6.2. | In observational study, were interventions, study settings, and clinicians/provider described? | Yes |
| 6.3. | Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect? | Yes |
| 6.4. | Was the amount of exposure and, if relevant, subject/patient compliance measured? | N/A |
| 6.5. | Were co-interventions (e.g., ancillary treatments, other therapies) described? | N/A |
| 6.6. | Were extra or unplanned treatments described? | N/A |
| 6.7. | Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups? | N/A |
| 6.8. | In diagnostic study, were details of test administration and replication sufficient? | N/A |
| **7.** | **Were outcomes clearly defined and the measurements valid and reliable?** | Yes |
| 7.1. | Were primary and secondary endpoints described and relevant to the question? | Yes |
| 7.2. | Were nutrition measures appropriate to question and outcomes of concern? | Yes |
| 7.3. | Was the period of follow-up long enough for important outcome(s) to occur? | Yes |
| 7.4. | Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures? | Yes |
| 7.5. | Was the measurement of effect at an appropriate level of precision? | Yes |
| 7.6. | Were other factors accounted for (measured) that could affect outcomes? | Yes |
| 7.7. | Were the measurements conducted consistently across groups? | Yes |
| **8.** | **Was the statistical analysis appropriate for the study design and type of outcome indicators?** | Yes |
| 8.1. | Were statistical analyses adequately described and the results reported appropriately? | Yes |
| 8.2. | Were correct statistical tests used and assumptions of test not violated? | Yes |
| 8.3. | Were statistics reported with levels of significance and/or confidence intervals? | Yes |
| 8.4. | Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)? | N/A |
| 8.5. | Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)? | Yes |
| 8.6. | Was clinical significance as well as statistical significance reported? | Yes |
| 8.7. | If negative findings, was a power calculation reported to address type 2 error? | N/A |
| **9.** | **Are conclusions supported by results with biases and limitations taken into consideration?** | Yes |
| 9.1. | Is there a discussion of findings? | Yes |
| 9.2. | Are biases and study limitations identified and discussed? | Yes |
| **10.** | **Is bias due to study's funding or sponsorship unlikely?** | Yes |
| 10.1. | Were sources of funding and investigators' affiliations described? | Yes |
| 10.2. | Was the study free from apparent conflict of interest? | Yes |